REMARKS

Claims 1-3, 10-16 and 45 remain before the Examiner for reconsideration. Claims 4-9 and 17-44 have been canceled without prejudice. Claims 1, 10, 11 and 45 have been amended herein as indicated above. Additions to the claims are indicated by underling the text added, and deletions from the claims are indicated by striking through the text deleted.

In the Office Action dated October 30, 2002, the Examiner withdrew several objections and rejections set forth in the pervious Office Action. Specifically, the Examiner indicated that:

> The objection to the Abstract is withdrawn in view of applicant's submission of a new Abstract. The rejections under 35 U. S. C. 112, second paragraph are withdrawn in view of applicant's claim amendments. Also, the rejections under 35 U.S.C. 102 and 103 are withdrawn in view of applicant's arguments. However, new rejections are made. Since the new rejections were not entirely necessitated by amendment to the claims, the case remains in non-final status.

The Examiner further indicated that "Applicant's arguments filed August 12, 2002 were found persuasive with respect to the Still et al reference and the rejections based on this reference are withdrawn.."

With respect to the previous restriction requirement and subsequent election by Applicants, the Examiner indicated that:

> As stated in the Restriction Requirement, claim 1 contains four different inventions. Applicant elected to examine, with traverse, the invention of Group I (claims 1 (in part), 2, 3, 10, 11-16 and 45). The traversal was addressed in the last Office Action and the Restriction Requirement was made final. In the previous Office Action (paragraph 7), the examiner stated that claim 1 is examined to the extent of the elected subject matter only. Thus the rest of claim 1, pertaining to the non-elected inventions, should be considered as withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions (the requirement having been traversed in Paper No. 6). Applicant has cancelled claims 4-9 and 17-44 as drawn to non-elected inventions; however, claim 1 has not been amended to remove the non-elected

> inventions contained within the claim. An amendment to remove the non-elected subject matter from claim 1 is respectfully requested. Please also see Objection below.

Applicants have amended Claim 1 to remove non-elected inventions.

The Examiner further objected to Claim 1, asserting that "As stated above (paragraph 4), claim 1 contains four inventions. Restriction within claim 1 was set forth in the Restriction Requirement. Applicant has not amended this claim to remove the non-elected subject matter." As set forth above, Applicants have amended Claim 1 to remove non-elected inventions, thereby obviating the Examiner's objections.

The Examiner rejected Claims 1 (in part), 2, 10, 11, 12, 14, 15 and 45 under 35 U.S.C. Section 102(e) "as being anticipated by Hochlowski et al (US 6,168,913) as evidenced by Webster's Dictionary (1994)." Specifically, the Examiner asserted:

> Hochlowski et al discloses "coding combinatorial chemical libraries synthesized on a plurality of solid supports by attaching "tags" that comprise fluorine containing compounds in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine nuclear magnetic resonance spectroscopy..." (see Abstract). Various fluorine containing tags are disclosed by the reference (see column 5, line 15 through column 13, line 21); these read directly on the claimed fluorous {tagging} moieties that differ in fluorous content or structure of instant claims 2, 12 and 15.
>
> The reference discloses using FNMR to identify the tags (see, for example, column 3, lines 2-21 and column 23, lines 1-14), creating for each solid support a code that generates "an unique FNMR spectrum" (column 4, lines 410). Note that for the purposes of this rejection that the term "separating" is given the art-recognized definition of "to discriminate or differentiate between", as evidenced by Webster's Dictionary. Thus, Hochlowski et al discloses "separating" the compounds of their coded libraries as the FNMR spectrum clearly differentiates between the tagged library members (see, for example, column 23, lines 1-14, Example 2 and patented claims). The separation discussed above is based on differences between the FNMR chemical shifts of the tagging moieties, see column 5, line 15 through column 13, line 21 {especially column 5, line 291 and Figures. This also reads on the "differences in fluorous nature" in instant claims 1, 11 and 14 and also on the "differences between the first tagging moiety and the second tagging moiety" in instant claim 45. Lastly, as the chemical shifts of the tags are known, the "order" of separation (i.e.

> placement of peaks in the FNMR spectrum) to identify the compounds that are tagged is deemed to be "predetermined", as recited in instant claims 10 and 45.

Applicants respectfully traverse the Examiner's rejections.

Hachlowski et al. discloses a method encoding combinatorial chemical libraries synthesized on a plurality of solid support (a polymeric bead) by attaching tags to the solid supports that comprise fluorine containing compounds. The tags can be decoded while attached to the solid support/polymeric bead by fluorine nuclear magnetic resonance (FNMR) spectroscopy to follow the reaction history of individual beads and to determine the particular member of the library that is attached to the polymeric bead.

Unlike the present invention and contrary to the Examiner's assertion, nowhere does Hachlowsik et al. disclose or suggest a separation of the polymeric bead based upon differences in the tags attached thereto. Indeed, given the extremely high molecular weight of such polymeric beads, there is no known separation technique via which such a separation could be accomplished. FNMR spectroscopy can be used only to identify different beads based upon different encoded tags.

The Examiner is simply incorrect in asserting that "for the purposes of this rejection that the term 'separating' is given the art-recognized definition 'to discriminate or differentiate between', as evidenced by Webster's Dictionary. One skilled in the art of the present invention would not give the terms 'separating' or 'separation' as used in the present claims the definition provided by the Examiner. Indeed, Hawley's Condensed Chemical Dictionary, Thirteenth Edition, R. J. Lewis, editor, Van Norstrand Reinhold, New York, New York (1997) provides a more appropriate definition of the term "separation" as used in the relevant art as: "A collective term including a large number of unit operations that, in one way or another, isolate the various components of a mixuture." Thus, as the term "separation" is used in the relevant art and as such term is clearly used in the present claims, Hachlowski et al. does not disclose or suggest a separation of the polymeric bead thereof based upon differences in the tags attached thereto.

The Examiner rejected Claim 45 under 35 U.S.C. Section 102(b) "as being anticipated by Brenner (US 5,604,097).." Specifically, the Examiner has asserted that:

> Brenner discloses "a method of tracking, identifying, and/or sorting classes or subpopulations of molecules by the use of oligonucleotide tags" (see Abstract). The "sorting" of Brenner reads on the claimed "separating". Specifically, see patented claim 1 of the reference. The method disclosed in this claim reads on instant claim 45 where "each polynucleotide in a population of polynucleotides" reads on the first and second compounds of the claims and the "oligonucleotide tags" read on the claimed tagging moieties. Each polynucleotide has a different oligonucleotide tag attached thereto (column 35, lines 3-5) and the polynucleotides from the population are sorted based on the hybridization of the tags (i.e. separated based upon "differences between the first tagging moiety and the second tagging moiety" as in instant claim 45). The hybridization events are controlled by the position of the complements, which are spatially arrayed (column 35, lines 15-19), reading on the "predetermined fraction" of the instant claim.

Applicants respectfully traverse the Examiner's rejections.

As set forth by the Examiner, Brenner discloses a method of tracking, identifying and/or sorting classes or subpopulations of molecules by the use of oligonucleotide tags. Nowhere does Brenner disclose or suggest a method of preparation for a fluorous separation wherein different fluorous tags are attached to compound to effect a subsequent fluorous separation as claimed in Claim 45 as amended.

The Examiner further rejected Claims 1 (in part), 2, 3, 10-16 and 45 under 35 U.S.C. 103(a) "as being unpatentable over Curran et al (US 5,859,247; of record) and Hochlowski et al (US 6,168,913)". Specifically, the Examiner asserted that:

> Curran et al teach separation techniques where "organic/fluorous phase separation techniques are used to effect separations" (see Abstract). These techniques are defined in column 3, line 35 - column 4, line 4 of the reference and read on the separations of instant claims 1, 2, 11, 12, 14 and 15, especially with respect to tagging moieties that differ in fluorous content. Fluorous reversed phase chromatography is specifically described, column 3, line 49 - column 4, line 4 (reading on claims 3, 13 and 16). Curran et al teach that these methods are preferred for separations (and synthesis) of combinatorial libraries (see column 8, line 50 - column 9,

line 32). The reference also teaches that a "plurality of fluorous moieties" can be used "such that any fluorous reaction components ... are separable from the target organic product" (column 6, lines 29-43) and that "it may be desirable to have more than one tag per molecule, and these tags may be the same or different" (column 16, lines 49-50).

Curran et al lacks the specific teaching of using multiple fluorous tags and separations based on differences between them.

However, the use of multiple tags in the synthesis and analysis of combinatorial libraries was well established in the art at the time of filing. For example, Hochlowski et al teaches "coding combinatorial chemical libraries synthesized on a plurality of solid supports by attaching "tags" that comprise fluorine containing compounds in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine nuclear magnetic resonance spectroscopy..." (see Abstract). Various fluorine containing tags are taught by the reference (see column 5, line 15 through column 13, line 21); these read directly on the claimed fluorous {taggingl moieties that differ in fluorous content or structure of instant claims 2, 12 and 15

Hochlowski et al teaches using FNMR to identify the tags (see, for example, column 3, lines 2-21 and column 23, lines 1-14), creating for each solid support a code that generates "an unique FNMR spectrum" (column 4, lines 410). Thus, Hochlowski et al clearly teaches differentiating between the tagged library members using their FNMR spectrum (see, for example, column 23, lines 1-14, Example 2 and patented claims). The differentiation discussed above is based on differences between the FNMR chemical shifts of the tagging moieties, see column 5, line 15 through column 13, line 21 {especially column 5, line 291 and Figures. This also reads on the "differences in fluorous nature" in instant claims 1, 11 and 14 and also on the "differences between the first tagging moiety and the second tagging moiety" in instant claim 45. Lastly, as the chemical shifts of the tags are known, the "order" of separation (i.e. placement of peaks in the FNMR spectrum) to identify the compounds that are tagged is deemed to be "predetermined", as recited in instant claims 10 and 45.

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use multiple fluorous tags in the fluorous separations (i.e. reversed phase chromatography) of Curran et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Hochlowski et al regarding the use of multiple fluorine containing tags in order to separate and identify each library compound (see column 2, line 65 through column 3, line 21). Also, the methodology of Curran is advantageous for combinatorial synthesis and

> analysis for a variety of reasons (see column 8, line 28 through column 9, line 11), such as allowing for reactions to be conducted in homogeneous phases. One would have been further motivated and had a high expectation of success because the tags of both Curran et al and Hochlowski et al are fluorine containing compounds.

Applicants respectfully traverse the Examiner's rejections.

Curran et al. discloses the separation of a compound that has been tagged with a fluorous moiety from other non-fluorous, organic compounds. Curran et al. does not disclose or suggest the tagging of multiple organic compounds with different fluorous tags to effect a fluorous separation of such fluorous-tagged compounds as set forth in the present invention. Moreover, for the reasons set forth above Hachlowski et al. does not overcome the deficiencies of Curran et al. In that regard, one cannot arrive at the present invention by combining the disclosure of Curran et al. with the disclosure of Hachlowski et al. Once again, Hachlowski et al. uses tags containing fluorine merely to identify different polymeric beads using FNMR. Nowhere does, Hachlowski et al disclose or suggest a separation of such polymer beads based upon tags attached thereto.

The Examiner has also rejected Claims 1 (in part), 2, 3, 10, 11-16 and 45 under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 1-9 of US 5,859,247 (of record) in view of Hochlowski et al (US 6,168,913)." Specifically, the Examiner asserted that:

> An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In reGoodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).
>
> Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited claims in the patent and in the instant application encompass separations based on differences in fluorous nature. The instant method uses more than one tagging moiety, while the method of US 5,859,247 only recites one tagging moiety. However, the

> method instantly claimed would be obvious over that in claims 1-9 of US 5,859,247 because to use more than one tagging moiety (to aid in the separation) would be obvious to one of ordinary skill. This is demonstrated by the teachings of Hochlowski et al, which teach the differentiation of library members using a plurality of fluorine containing tags (see Abstract and column 5, line 15 through column 13, line 21).
>
> Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use multiple fluorous tags in the fluorous separations of Curran et al. A person of ordinary skill in the art would have been motivated to do so based on the teachings of Hochlowski et al regarding the use of multiple fluorine containing tags in order to separate and identify each library compound (see column 2, line 65 through column 3, line 21). One would have been further motivated and had a high expectation of success because the tags of both Curran et al and Hochlowski et al are fluorine containing compounds.

Applicants respectfully traverse the Examiner's rejections.

For the reasons set forth above with regard the Examiners rejection of the claims under Section 102 and 103 over Hochlowski et al. and/or Curran et al., the Applicants respectfully traverse the Examiner's rejection. Once again, Curran et al. discloses the separation of a compound that has been tagged with a fluorous moiety from other non-tagged non-fluorous, organic compounds. Curran et al. does not disclose or suggest the tagging of multiple organic compounds with different fluorous tags to effect a fluorous separation of such fluorous-tagged compounds as set forth in the present invention. Moreover, for the reasons set forth above Hachlowski et al. does not overcome the deficiencies of Curran et al. In that regard, one cannot arrive at the present invention by combining the disclosure of Curran et al. with the disclosure of Hachlowski et al. Once again, Hachlowski et al. uses tags containing fluorine merely to identify different polymeric beads using FNMR. Nowhere does, Hachlowski et al disclose or suggest a separation of such polymer beads based upon tags attached thereto.

In view of the above and remarks, the Applicants respectfully requests that the Examiner withdraw the objection to the Abstract, withdraw the rejections of the claims, indicate the allowability of the claims and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,

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IN THE CLAIMS:

Please amend the text of Claims 1, 11 and 45 as follows:

1. (Currently Amended) A method of separating compounds, the method comprising the steps of:

a. tagging at least a first organic compound with a first tagging moiety to result in a first tagged compound;

b. tagging at least a second organic compound with a second tagging moiety different from the first tagging moiety to result in a second tagged compound; and

c. separating the first tagged compound from a mixture including at least the second tagged compound using a separation technique based upon differences between the first tagging moiety and the second tagging moiety, the separation technique being based upon difference in fluorous nature of the first tagged compound and the second tagged compound~~, differences in total charge between the first tagged compound and the second tagged compound, differences in size between the first tagged compound and the second tagged compound, or differences in polarity between the first tagged compound and the second tagged compound~~.

2. (Original) The method of Claim 1 wherein the first tagging moiety and the second tagging moiety are fluorous moieties that differ in fluorous content or structure.

3. (Previously Amended) The method of Claim 2 wherein the first tagged compound and the second tagged compound are separated using fluorous reverse phase chromatography.

4. (Canceled)

5. (Canceled)

6. (Canceled)

7. (Canceled)

8. (Canceled).

9. (Canceled)

10. (Original) The method of Claim 1 wherein the first tagging moiety and the second tagging moiety are selected so that the order in which the first tagged compound and the second tagged compound separate is predetermined.

11. (Currently Amended) A method of separating compounds, the method comprising the steps of:

a. tagging at least a first organic compound with a first fluorous tagging moiety to result in a first tagged compound;

b. tagging at least a second organic compound with a second fluorous tagging moiety different from the first tagging moiety to result in a second tagged compound; and

c. separating the first tagged compound from a mixture including the second tagged compound using a separation technique based upon ~~upon~~ differences in the fluorous nature of the first tagged compound and the second tagged compound.

12. (Original) The method of Claim 11 wherein the first fluorous tagging moiety and the second fluorous tagging moiety differ in fluorine content or structure.

13. (Previously Amended) The method of Claim 12 wherein the first tagged compound and the second tagged compound are separated using fluorous reverse phase chromatography.

14. (Original) A method of separating compounds, the method comprising the steps of: tagging a plurality of organic compounds with a plurality of fluorous tagging moieties to result in a plurality of tagged compounds, each of the fluorous tagging moieties being different; and separating at least one of the plurality of

tagged compounds from other tagged compounds with a different tag using a separation technique based upon differences in the fluorous nature of the tagged compounds.

15. (Previously Amended) The method of Claim 14 wherein a first fluorous tagging moiety and a second fluorous tagging moiety of the plurality of fluorous tagging moieties differ in fluorine content or structure.

16. (Previously Amended) The method of Claim 15 wherein a first tagged compound[s] tagged with the first fluorous tagging moiety and a second tagged compound[s] tagged with the second fluorous tagging moiety are separated using fluorous reverse phase chromatography.

17. (Canceled)

18. (Canceled)

19. (Canceled)

20. (Canceled)

21. (Canceled)

22. (Canceled)

23. (Canceled)

24. (Canceled)

25. (Canceled)

26. (Canceled)

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Canceled)

40. (Canceled)

41. (Canceled)

42. (Canceled)

43. (Canceled)

44. (Canceled)

45. (Currently Amended) A method of ~~separating compounds~~ preparation for a fluorous separation from a mixture of compounds, the method comprising the steps of:

a. tagging a first organic compound with a first fluorous tagging moiety to result in a first fluorous tagged compound; and

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b. tagging at least a second organic compound with a second fluorous tagging moiety different from the first fluorous tagging moiety to result in a second fluorous tagged compound, the first fluorous tagging moiety being different from the first fluorous tagging so that the first fluorous tagged compound can be separated from the second fluorous tagged compound in the mixture of compounds including the first fluorous tagged compound and the second tagged fluorous compound using a separation technique based upon the differences in the fluorous nature of the first fluorous tagged compound and the second fluorous tagged compound.~~; and~~

~~c. separating the first tagged compound into a predetermined fraction from a mixture including at least the second tagged compound using a separation technique based upon differences between the first tagging moiety and the second tagging moiety, wherein the predetermined fraction and the identity of the first tagged compound in the predetermined fraction are determined by the first tagging moiety.~~